

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference JAB 1742-PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP 03/08694	International filing date (day/month/year) 05.08.2003	Priority date (day/month/year) 12.08.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/445		
Applicant JANSSEN PHARMACEUTICA N.V. et al.		



- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

 These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 05.02.2004	Date of completion of this report 08.11.2004
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Kollmannsberger, M Telephone No. +49 89 2399-7364 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/08694**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-27 as originally filed

Claims, Numbers

1-10 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/08694**

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-10
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-10
Industrial applicability (IA)	Yes: Claims	1-10
	No: Claims	

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP 03/08694

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V-1. Prior art

The following documents are considered relevant:

- D1: WO 01/97810 A (DAUGAN ALAIN CLAUDE MARIE ;KIRILOVSKY JORGE EDUARDO (FR); GLAXO GR) 27 December 2001 (2001-12-27)
- D2: WO 01/96327 A (DODIC NERINA ;GLAXO GROUP LTD (GB)) 20 December 2001 (2001-12-20)
- D3: WO 00/32582 A (DAUGAN ALAIN CLAUDE MARIE ;GLAXO GROUP LTD (GB)) 8 June 2000 (2000-06-08)
- D4: WO 02/20501 A (BACKX LEO JACOBUS JOZEF ;VEKEN LOUIS JOZEF ELISABETH V (BE); VIELL) 14 March 2002 (2002-03-14)

The P-document cited in the search report will be ignored during the international phase.

V-2. Novelty (Art. 33(2) PCT):

The claimed compounds differ from the compounds disclosed in D1-D3 in that the compounds of D1-D3 are either piperazines or, if piperidines, the piperidine is attached via a carbon atom to the benzene ring (cf. claims of D1-D3). The disclosure of D4 differs from the present claims in that the linking group A (nomenclature of D4) has an obligatory cyclic substituent whereas in the present claims (if present) it is an unsubstituted methylene group. The claims are thus novel.

V-3. Inventive step (Art. 33(3) PCT):

The present application deals with compounds which inhibit the secretion of apolipoprotein B and thus lower the LDL-level in blood. D1-D4 are concerned with the same problem. The problem to be solved can be seen in the provision of further

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP 03/08694

compounds presenting this activity.

D1-D3, which can be regarded as closest state of the art, disclose compounds (see example compounds mentioned in the search report) that differ from the present claims only in that they are piperazines instead of piperidines. From D4 (see definition of X in the claims and e. g. compound 30, p. 69 compared with compound 145, p. 78 with corresponding activity data in table C1 p. 90-92) it is clear that piperidines and piperazines are equivalents. It was thus obvious for a skilled man that the claimed compounds would present the same activity.

An inventive step could only be considered if the claimed compounds were the solution to a different problem derivable from the description, e. g. the problem of finding compounds that unexpectedly show improved properties vis-a-vis the compounds of D1-D3. It is not apparent that such a problem has been solved.

The claims do not fulfil Art. 33(3) PCT.